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Acute liver failure in an adolescent after intentional ingestion of paracetamol with suicidal ideation: a case report

Falência hepática aguda em adolescente após ingestão proposital de paracetamol com ideação suicida: um relato de caso

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ABSTRACT

Presently, paracetamol stands as one of the most widely consumed analgesic and anti pyretic medications within society. This prevalence is attributed to its non-prescription status and cost-effectiveness, facilitating widespread accessibility. This report delineates a case of paracetamol poisoning culminating in liver failure, necessitating liver transplantation. The subject, a thirteen-year-old with suicidal ideation, ingested 15 tablets of 750 mg. Initial treatment occurred at a Primary Health Care Unit in a municipality in the interior of Rio Grande do Sul, followed by pediatric ICU care at the University Hospital of the Federal University of Rio Grande. Subsequently, the patient was transferred and managed at the Hospital de Clínicas de Porto Alegre, where a successful transplant ensued. Post-transplant, the patient received tacrolimus (10mg orally twice daily), prednisone (5mg orally twice daily), and Sulfametoxazol + Trimethoprim (400 + 80 mg) thrice weekly for maintenance. This case underscores the pivotal role of prompt intervention, fostering awareness regarding judicious drug utilization, and advocating for more stringent regulations pertaining to over-the-counter medication accessibility.

Keywords: Case report; Acetaminophen; Intoxication; Liver transplantation; Pediatrics.

RESUMO

Atualmente, o paracetamol é um dos medicamentos analgésicos e antipiréticos mais consumidos pela sociedade, devido a isenção de prescrição médica e baixo custo, possibilitando maior facilidade de aquisição. O presente relato descreve um caso de intoxicação por paracetamol com evolução para insuficiência hepática e necessidade de transplante hepático. O caso descrito foi de uma adolescente de treze anos de idade, que ingeriu 15 comprimidos de paracetamol de 750 mg, com ideação suicida. A paciente foi atendida em uma Unidade de Saúde em um município do interior do Rio Grande do Sul, sendo transferida posteriormente para a UTI pediátrica do Hospital Universitário da Universidade Federal de Rio Grande, e posteriormente transferida e acompanhada pelo Hospital de Clínicas de Porto Alegre, onde realizou o transplante, teve boa aceitação do enxerto e começou a fazer uso dos imunossupressores tacrolimo 10mg via oral duas vezes ao dia, prednisona 5mg via oral 2 comprimidos ao dia e sulfametoxazol + trimetoprima (400 + 80 mg) três vezes na semana para manutenção. Ressalta-se a importância da intervenção precoce, conscientização sobre o uso racional de medicamentos e a necessidade de regulamentações mais rigorosas para o acesso a medicamentos de venda livre.

Palavras-chaves: Relato de caso; Paracetamol; Intoxicação; Transplante hepático; Pediatria

Introduction

Approximately 27% of poisonings in Brazil are caused by medications. Of these, nearly a quarter occur by accident, and half are due to suicide attempts. Undoubtedly, the available evidence allows for establishing a correlation between self-medication and the widespread accessibility of over-the-counter medications. This practice has significant implications in the context of public health, thus outlining the imperative need to adopt educatioanal and regulatory measures aimed at mitigating the intrinsic risks associated with self-medication.[1,2,3]

Self-destructive behaviors, such as self-mutilation, can trigger suicidal ideation. In adolescence, issues related to identity, family problems, and trauma can lead to impulsive acts. Easy access to medications at home, especially paracetamol, other analgesics, and antidepressants, stands out as a contributing factor to the risk of fatal outcomes if appropriate treatment is delayed.[4,5,6]

Based on this scenario, the present study aims to present a case report of a 13-year-old adolescent who experienced acute paracetamol poisoning with suicidal ideation and significant clinical consequences. This case report originates from a descriptive prospective cohort study conducted at the Hospital de Clínicas de Porto Alegre (HCPA), which has approximately 900 beds.

The research was submitted through the Plataforma Brasil to the Ethics and Research Committees of the Hospital de Clínicas de Porto Alegre (CEP - HCPA) and the Federal University of Rio Grande do Sul (UFRGS) and was approved under number 3.458.868.

Case Report

A 13-year-old female adolescent, weighing 63 kg and measuring 1.64 meters in height, originally from the interior of Rio Grande do Sul, was admitted to the Hospital de Clínicas de Porto Alegre (HCPA) after four days of a probable suicide attempt by ingesting 15 tablets of paracetamol (750 mg). The patient presented with acute liver failure and underwent an emergency liver transplant six days after the ingestion of the tablets. She experienced the loss of her father at the age of six, which left her in a melancholic and depressive state. She would sleep holding her father's photo and frequently visited the cemetery.

The mother of the child noticed depressive signs in the adolescent, observing a decline in her school performance to the point where she no longer wanted to attend school. She also exhibited signs of self-harm, such as cuts on her arms and legs. After these observations, the mother took her daughter to a psychiatrist who prescribed antidepressants. The treatment lasted only one month, as the mother stopped it upon discovering that her daughter had taken four tablets at once to help her sleep, and referred her to a health unit for a psychological evaluation, which did not follow up.

There is a family history of suicide. The mother reported that she did not know how to handle the situation and at times felt irritated by the circumstances they were facing. These feelings contributed to a strained bond with her daughter, making it difficult to manage the adolescent's needs.

On the day of the overdose and intoxication, the adolescent did not exhibit any behavioral changes; she even visited relatives during the day. In the evening, she ingested 15 tablets of paracetamol (750 mg) and subsequently experienced epigastric pain and vomiting, informing her mother about the incident approximately two hours after ingestion. Following this, the mother sought care at the Santa Casa de Rio Grande Health Unit (USSCRG), where she was hospitalized for two days.

Exams were conducted at USSCRG, and during observation, she remained without sensory alterations, only complaining of abdominal pain and nausea. The following day, N-acetylcysteine was prescribed (**item A.1., Table 1**), but the patient vomited after ingestion.

On the second day, she presented with jaundice and dark urine. Hemogram and liver enzyme tests were repeated, and clinical deterioration was noted, leading to her transfer to the pediatric ICU at the University Hospital of the Federal University of Rio Grande (HU-FURG). Management was initiated with oral administration of N-acetylcysteine, but without success. On the third day, there was further clinical worsening, with disorganized speech, altered sensorium, and acute renal injury, resulting in her transfer to HCPA on the fourth day after the exposure.

Table 1. Critical Analysis of Medications Prescribed During Patient's Progression

Prescription	Description of dose and reason for use
A. During hospitalization at FURG Hospital	
A.1. N–Acetylcysteine 600mg orally	Attack dose: 8,400mg (14 sachets) Maintenance dose: 7 sachets every 4 hours Antidote for paracetamol poisoning
B. During hospitalization at HCPA	
B.1. N–Acetylcystenine 600mg oralle	Attack dose: 150mg/kg (9,450 mg) in one hour Maintenance dose: 50mg/kg (3,150mg) in four hours for seconde dose Maintenance dose: 100mh/kg (6,300mg) in sixteen hours for third dose Antídoto para intoxicação com paracetamol.
B.2. Midazolam 5mg/mL	Dose: Administer 1 mL intravenously every 4 hours. Treatment for seizure crisis.
B.3. Phenytoin 50mg/mL	Attack dose: 1 gram intravenously. Maintenance dose: 100 mg intravenously every 12hours. Treatment for seizure crisis.
B.4. Albumin 20% 20 mg/mL (50 mL)	Dose: 1 vial, intravenously 3 times a day. Administered for dialysis with a single passage.
B.5. Cefepime 2 grams	Dose: 2 grams intravenously every 8 hours Administered for antimicrobial prophylasis.
B.6. Methylprednisolone succinate 500 mg	Dose: 125 mg intravenously once a day. Administered for prophylaxis against liver transplant rejection
B.7. Vancomicyn 500 mg	Dose: 500 mg intravenously every 12 hours. Administered for antimicrobial prophylasis.
B.8. Omeprazole 40 mg	Dose: 40 mg intravenously once a day. Administered for gastric discomfort.
C. After Transplant	
C.1. Acetylsalicylic Acid 100mg	Dose: 1 tablet via tube once a day. Administered to prevent platelet aggregation.
C.2. Tacrolimus 10mg	Dose: 10 mg orally every 12 hours. Immunosuppressant to prevent liver transplant rejection.
C.3. Sulfamethoxazole+ Trimethoprim (400 + 80 mg)	Dose: 1 tablet Administered for antibacterial prophylaxis.
C.4. Omeprazole 20 mg	Dose: 20 mg 1 once a day. Administered for gastritis prophylaxis.
C.5. Prenisona 5 mg	Dose: 2 tablets orally once a day. Administered to assist in immunosuppression.

Upon admission to the Hospital de Clínicas de Porto Alegre, another dose of N-acetylcysteine was initiated (**item B.1., Table 1**), but there was no improvement in the patient's condition. She presented as agitated, with episodes of conjugate gaze deviation, commissural deviation, pupils that were medium-sized, miotic, isocoric, and reactive to light, along with hypertonia, which configured a convulsive crisis. This crisis was resolved after the administration of midazolam 5 mg/mL and phenytoin 50 mg/mL (**items B.2. and B.3., Table 1**).

With the continuous worsening of transaminases (**Table 2**), the patient progressed to hepatic failure, with an increase in total and direct bilirubin. Conse-

quently, she was placed on the liver transplant waiting list as a priority due to the severity of her clinical condition.

On the fourth day, the patient received platelet concentrate, plasma, and initiated dialysis with albumin (**item B.4., Table 1**) in a single pass, due to the severity of the intoxication and encephalopathy. Despite a partial improvement in coagulation factors after plasma administration, there remained laboratory evidence of hepatocellular injury, worsening bilirubin levels (**Table 2**), and severe hepatic encephalopathy, maintaining the indication for transplantation.

A compatible donor organ was offered, and on the sixth day, a liver transplant was performed. The patient had a good recovery post-transplant, and after two months, there was adequate graft function, with normal transaminases, blood pressure appropriate for her age, and no need for antihypertensive medication.

After the organ graft, the patient was on a daily regimen of 100 mg of acetylsalicylic acid, 10 mg of tacrolimus, 480 mg of sulfamethoxazole + trimethoprim, 20 mg of omeprazole, and 5 mg of prednisone (**items C.1., C.2., C.3., C.4., C.5., Table 1**).

Eleven months after the transplant, the use of acetylsalicylic acid and sulfamethoxazole + trimethoprim was suspended, and the maintenance dose of tacrolimus was adjusted to 7 mg every 12 hours. Despite the patient displaying an apparently euphoric mood due to some disappointments regarding restrictions related to the transplant, there is good adherence to the treatment, particularly with the immunosuppressant tacrolimus.

Discussion

There is a potential for severe hepatic damage in adults when the intake of acetaminophen is approximately 12 g or more, and in children, the potentially harmful dose is about 200 mg of acetaminophen per kg.[7] The patient in this case ingested 11.25 g, which is considered a high dose with the potential for severe hepatic damage.

The first symptoms presented by the patient are described in phase 1 of the poisoning, characterized by nausea and abdominal pain within a few hours after ingesting the medication.[7] The tests performed on the patient upon admission to HU-FURG, two days after exposure, revealed an increase in liver enzymes: AST 8,598 U/L (reference 5-34 U/L) and ALT 2,034 IU/L (reference less than 55 U/L), along with an INR of 7.46 (reference 0.8 – 1), indicating a hemorrhagic risk. These laboratory findings demonstrate acute intoxication 24 hours after exposure to acetaminophen, as the drug is metabolized through sulfation and glucuronidation. When these pathways are saturated, the secondary pathway involves cytochrome P450, particularly CYP2E1, which generates a toxic metabolite, N-acetyl-p-benzoquinoneimine (NAPQI).[8] This is immediately detoxified by glutathione into mercapturic acid (non-toxic), which is naturally eliminated in urine. When glutathione is depleted, NAPQI binds to cellular proteins, leading to hepatocyte necrosis and increased transaminases.[8]

In the second phase of intoxication, the clinical changes indicate real toxicity, with hepatocellular injury. On the third day after exposure, there is a continued elevation of transaminases and acute renal injury (Table 1).[9]

On the fourth day, neurological symptoms emerged, including seizures and pupils that were mid-size, miotic, isocoric, and reactive to light, marking the third phase of intoxication, with the risk of coma and damage to organs such as the pancreas, kidneys, and heart.[9]

On the first day, still at HU-FURG, the patient was treated with N-acetylcysteine to combat acetaminophen overdose and hepatic damage. This antidote acts as a substitute for glutathione, eliminating NAPQI into mercapturic acid. However, the patient was unable to tolerate the treatment due to constant vomiting, resulting in hepatic failure (evidenced by worsening bilirubin levels and severe hepatic encephalopathy) and the need for organ transplantation.[9,10,11,12] At the FURG Hospital, the patient received a loading dose of 8,400 mg of N-acetylcysteine orally (140 mg/kg), followed by a maintenance dose of 4,200 mg (70 mg/kg). On the third day, she was transferred to HCPA, where she received a new loading dose of 9,450 mg (150 mg/kg) administered over one hour, followed by a maintenance dose of 3,150 mg (50 mg/kg) over four hours and another dose of 6,300 mg (100 mg/kg) over sixteen hours. On the sixth day, the transplant was performed.

Table 2. Monitoring of the patient's biochemical parameters during hospitalization at HCPA and after liver transplantation.

Time after hospitalization at HCPA	AST 5-34 U/L	ALT 55 U/L	GGT 8-33 U/L	Direct bilirubin 0,5 mg/L	Indirect bilirubin 0,7 mg/dL	Total bilirubin 0,3-1,2 mg/dL	Alkaline phosphatase 141-460 U/L	Creatinine 0,57–1,11 mg/dL
Dia 1	6154	8457	83	4,6	2,3	6,6	158	1,68
Dia 2	1276	3702	87	4,9	2,2	7,1	115	0,96
Dia 3	3961	3560	109	3,1	1,1	4,2	68	1,47
Dia 4	437	2454	121	1,3	0,5	1,8	71	1,59
Dia 5	297	1684	109	0,8	0,4	1,2	67	1,52
Dia 6*	120	1227	176	0,7	0,1	1	87	1,25
Dia 7	62	846	170	0,6	0,3	0,9	70	1,1
Dia 8	44	574	167	0,5	0,3	0,8	84	0,78
Dia 9	65	438	254	0,5	0,3	0,8	111	0,69
Dia 21	20	116	274	0,3	0,2	0,5	101	0,56
1 mês	19	77	177	0,2	0,2	0,4	92	0,56
2 meses	15	34	97	0,1	0,2	0,3	59	0,7

*Day the liver transplant was performed

Patients undergoing liver transplantation after intentional ingestion and with a history of psychological disorders require psychiatric follow-up to provide social and family support, preventing complications to the graft and optimizing the use of limited resources. Upon receiving the transplanted organ six days after exposure, the patient had a good postoperative evolution and began immunosuppression with 10 mg/day of tacrolimus orally. This drug inhibits T lymphocytes and is metabolized in the liver via CYP3A4 and is not dialyzable. Despite being essential, its use increases morbidity and mortality (potential nephrotoxic), highlighting the need for strict monitoring throughout the patient's life.[13]

Eleven months after the transplant, the patient showed good acceptance of the liver graft and good adherence to treatment; however, she appeared anxious due to the limitations that the transplant imposed on her routine.

The condition presented by the patient, including the need for liver transplantation, is consistent with other similar reports described in the literature[14-16], including those regarding the antidote used[17,18] to attempt to contain the clinical progression of the intoxication.

Transplanted patients, subject to multiple medications, including immunosuppressants and prophylactics against opportunistic infections, require pharmacotherapy monitoring. The multidisciplinary team, especially the pharmacist, plays a crucial role in the postoperative period to minimize the risks of interactions and adverse reactions, ensuring treatment adherence, optimizing pharmacotherapy, and enhancing the patient's quality of life.[19,20]

As liver transplantation is fully subsidized by the Unified Health System and is a high-complexity procedure that incurs significant costs, it is used as a last treatment option for terminal patients. Therefore, it is essential to prevent graft rejection and increase both graft and patient survival through proper pharmacotherapy monitoring.[21]

Final Considerations

The indiscriminate use of medications carries risks. The abundant availability of these products and easy access lead to self-medication and the possibility of suicide attempts by vulnerable individuals. Acute intoxication from paracetamol can result in liver failure and may require transplantation at doses greater than 12 g in adults and 200 mg/kg in children. There is a need to reflect on health education interventions for various levels of human life in order to address this pressing issue, as well as a reformulation of sanitary regulation to restrict or provide greater safety for the use of over-the-counter medications.

Contributions of the Authors
SD: investigation and writing; GRMF: review and editing; IH: review and editing; SZ: data curation, formal analysis, methodology, and supervision; DG: data curation, formal analysis, methodology, supervision, and review.

Conflicts of Interest
The authors declare that there are no conflicts of interest.

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21. Portela MP, Neri EDR, Fonteles MMF, Garcia JHP, Fernandes MEP. The cost of liver transplantation in a university hospital in Brazil. Rev Assoc Med Bras. 2010; 56 (3): 322–6. Table 1. Critical analysis of the medications prescribed during the patient's evolution.